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Electrical Systole (Q-T Interval) of Rabbit Heart.

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The QT interval of the electrocardiogram encompasses the whole of activation and recovery of the ventricular muscle. Its duration varies with the heart rate. Logarithmic curves relating the QT interval to the preceding cycle length have been drawn by numerous authors;[1,2] a recent paper[3] attempts to establish a linear QT-RR relationship. The QT interval is prolonged in many varieties of heart disease, by myocardial anoxemia, by diminution in the blood calcium level, and by quinidine. Administration of digitalis shortens the QT interval, particularly when it has been prolonged by myocardial disease. Robb[4] has recently suggested that extra-cardiac factors may reflexly influence the QT duration.

In human patients, or in intact animals, the feasible variations in heart rate are limited. Hence we have studied the QT-RR relationship in the isolated perfused rabbit ventricle, using the technic previously described,[5] which permits variation in rate from that of the idioventricular pacemaker, 50-100/min., up to 400/min. or more. Strophanthin was injected into the perfusion system in doses approximating 0.006 mg/kilo of intact rabbit; then quinidine was employed in a dose of 0.15 mg/kilo. The effect of these drugs on electrical systole was studied.

Results. The figures show the forms of QT-RR curves obtained from this preparation. The QT interval is often prolonged by changes from very slow to moderate rates; further increasing rates uniformly shorten the QT measurement. The curve often flattens out at extremely rapid ventricular rates.

Quinidine, as has often been shown, always prolongs the QT interval markedly (Fig. 1).

The effect of strophanthin-K (Strophosid, Sandoz) was variable. When used in the above dosage, there was in some preparations prolongation of the QT interval; just as often shortening was obtained; several showed no appreciable change from the control curves. It was then found that when small amounts of strophanthin prolonged the QT interval, larger doses shortened it (Fig. 2).*

Comment. The QT-RR curves obviously are not linear, although in the central portion, excluding the slowest and fastest rates, the deviation from linearity may not be great. We have not attempted to derive formulæ that might fit the curves obtained.

If the QT interval measures, in its first part, intraventricular conduction, but in its greater portion, ventricular refractoriness, it is readily understood why increasing rates should shorten the QT duration, up to a limit at which further shortening becomes impossible. It is difficult, however, to explain on a similar basis the occasional slight prolongation of QT at moderate, as compared to very slow rates.

Clark and Mines[6] noted that strophanthin first prolonged, later shortened, the duration of the electrical response of the isolated frog heart. In human subjects, only the shortening has been observed to follow therapeutic dosage of digitalis glucosides. It appears that prolongation of the QT interval has been demonstrated only in isolated hearts; whether or not it may be found early in the course of gradual digitalization of humans has not yet been

[1] Albers, D., and Bedbur, W., *Arch. f. Kreislauffforschung*, 1941, **8**, 150.

[2] Ashman, R., PROC. SOC. EXP. BIOL. AND MED., 1939, **40**, 150.

[3] Schlamowitz, I., *Am. Heart J.*, 1946, **31**, 329.

[4] Robb, J. S., *Fed. Proc.*, 1946, **5**, 87.

[5] Decherd, G. M., and Ruskin, A., PROC. SOC. EXP. BIOL. AND MED., 1946, **63**, 114.

* Since the submission of these papers, we have been able to demonstrate similar effects of small and large doses of Cedilanid (Sandoz) and Scillaren-B (Sandoz), as well as digitoxin.

[6] Clark, A. J., and Mines, G. R., *J. Physiol.*, 1913, **47**, vii.

[7] Kisch, B., *Strophanthin*, Brooklyn Medical Press, 1944.

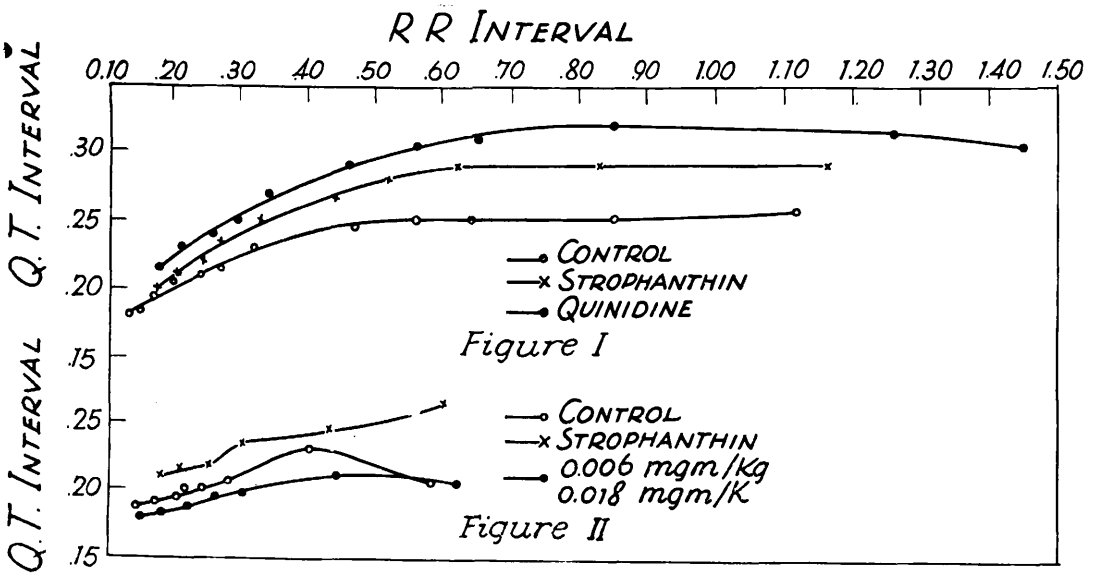

FIG. 1.
Curves relating the QT interval to the cycle length. The effect of digitalis and of quinidine for one experiment is shown.

FIG. 2.
QT-RR curves for a small, and for a large, dose of strophanthin.

determined. Strophanthin has been found,[7] like digitalis, to shorten the QT interval in animal experiments and in human patients. Although the action of quinidine in prolonging refractoriness, *i. e.*, the QT interval, parallels its effect in delaying intraventricular conduction as measured by the width of the QRS complex,[5] this parallelism is lacking for strophanthin, at least in the larger doses.

At fast rates strophanthin and quinidine produce relatively little deviation from the control curve; the effects of increased rates apparently minimize the influence of the drug. Conversely, the most marked changes in the QT interval, produced by these drugs, are usually noted at relatively slower rates of stimulation.

Summary. Curves have been drawn relating the QT interval to the cycle length for the isolated perfused rabbit ventricle. The effect of strophanthin and of quinidine on these curves has been studied.

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Effect of Mustard Gas on Mitosis and P^{32} Uptake in Regenerating Liver.*

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Rats (1 month, 40-50 g) were partially hepatectomized and 24 hours later β*is* (β-chloroethyl) sulfide ("HS") was injected into the femoral vein. The HS was dissolved in propylene glycol, at a concentration of 2 mg per cc. (A dose of 2 mg per kilo killed rats in 3-4 days.) Ten minutes later P^{32} as Na_2HPO_4 was administered intra-

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